

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:** Please amend the claims as follows:

**We claim:**

**Claim 1. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which modulates the biological function of one or several of the Angiopoietin/Tie receptor systems.

**Claim 2. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which is targeted to the endothelium via of one or several of the VEGF/VEGF receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which modulates the biological function of one or several of the Angiopoietin/Tie receptor systems.

**Claim 3. (Cancelled)**

**Claim 4. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which is targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

**Claim 5. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which is targeted to the endothelium via one or several of the VEGF/VEGF receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which is

targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

**Claim 6. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which modulates the biological function of one or several of the VEGF/VEGF receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which are is targeted to the endothelium via one or several of the VEGF/VEGF receptor systems.

**Claim 7. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition comprising ~~one or several agents~~ at least one agent as compound I which modulates the biological function of one or several of the Angiopoietin/Tie receptor systems, and further comprising ~~one or several agents~~ at least one agent as compound II which are is targeted to the endothelium via one or several of the Angiopoietin/Tie receptor systems.

**Claim 8. (Withdrawn)** Pharmaceutical compositions comprising one or several agents which interfere with both the function of one or several of the VEGF/VEGF receptor systems and the function of one or several of the Angiopoietin/Tie receptor systems.

**Claim 9. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition according to claim 1 which are is intended adopted for simultaneous or separate sequential ~~therapeutical~~ therapeutic application.

**Claim 10. (Currently Amended)** ~~Pharmaceutical compositions~~ A pharmaceutical composition according to claim 1 which comprises as compound I at least one of

- a) ~~compounds~~ a compound which inhibits receptor tyrosine kinase activity,
- b) ~~compounds~~ a compound which inhibits ligand binding to receptors,
- c) ~~compounds~~ a compound which inhibits activation of intracellular signal pathways of the receptors,
- d) ~~compounds~~ a compound which inhibits or activates expression of a ligand or

- of a receptor of the VEGF or Tie receptor system,
- e) ~~delivery systems, such as antibodies~~ a delivery system comprising an antibody, a ligands, a high-affinity binding oligonucleotides or oligopeptides, or a liposomes, which targets cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,
  - f) ~~delivery systems, such as antibodies~~ a delivery system comprising an antibody, a ligands, a high-affinity binding oligonucleotides or oligopeptides, or a liposomes, which ~~are~~ is targeted to the endothelium and induce necrosis or apoptosis.

**Claim 11. (Currently Amended)**      ~~Pharmaceutical compositions~~ A pharmaceutical composition according to claim 1 which comprises as compound II at least one of

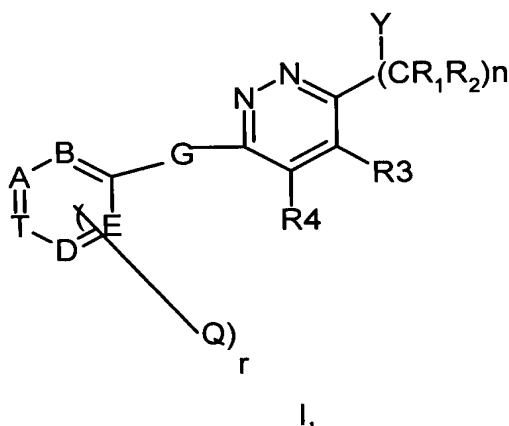
- f) ~~compounds~~ a compound which inhibits receptor tyrosine kinase activity,
- g) ~~compounds~~ a compound which inhibits ligand binding to receptors,
- h) ~~compounds~~ a compound which inhibits activation of intracellular signal pathways of the receptors,
- i) ~~compounds~~ a compound which inhibits or activates expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- j) ~~delivery systems, such as antibodies~~ a delivery system comprising an antibody, a ligands, a high-affinity binding oligonucleotides or oligopeptides, or a liposomes, which targets cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,
- k) ~~delivery systems, such as antibodies~~ a delivery system comprising an antibody, a ligands, a high-affinity binding oligonucleotides or oligopeptides, or a liposomes, which ~~are~~ is targeted to the endothelium and induce necrosis or apoptosis.

**Claim 12. (Withdrawn)**      Pharmaceutical compositions according to claim 1 which comprise as compound I and/ or II at least one of Seq. ID Nos. 1-59.

**Claim 13. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II SEQ ID NO:60.

**Claim 14. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I and/ or II at least one of sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTFconjugate.

**Claim 15. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I and/ or II at least one small molecule of general formula I



in which

r

has the meaning of 0 to 2,

n

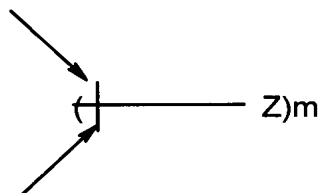
has the meaning of 0 to 2;

R<sub>3</sub> und R<sub>4</sub>

a) each independently from each other have the meaning of lower alkyl,

b) together form a bridge of general partial formula

II,

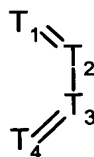


II,

wherein the binding is via the two terminal C- atoms,  
and

m has the meaning of 0 to 4; or

c) together form a bridge of partial formula III



III,

wherein one or two of the ring members  $T_1, T_2, T_3, T_4$  has  
the meaning of nitrogen, and each others have the  
meaning of CH, and the binding is via the atoms  $T_1$  and  $T_4$ ;

G has the meaning of  $C_1 - C_6$  - alkyl,  $C_2 - C_6$  - alkylene or  
 $C_2 - C_6$  - alkenylene; or  $C_2 - C_6$  - alkylene or  $C_3 - C_6$ -  
alkenylene, which are substituted with acyloxy or  
hydroxy;  $-CH_2-O-$ ,  $-CH_2-S-$ ,  $-CH_2-NH-$ ,  $-CH_2-O-CH_2-$ ,  
 $-CH_2-S-CH_2-$ ,  $-CH_2-NH-CH_2$ , oxa ( $-O-$ ), thia ( $-S-$ ) or  
imino ( $-NH-$ ),

A, B, D, E and T independently from each other have the meaning of N  
or CH, with the proviso that not more than three of  
these Substituents have the meaning of N,

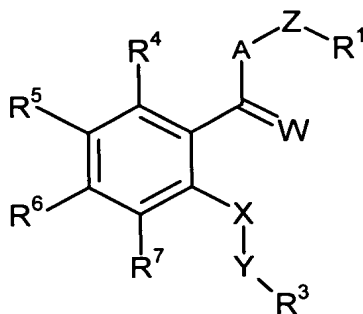
Q	has the meaning of lower alkyl, lower alkyloxy or halogene,
R <sub>1</sub> and R <sub>2</sub>	independently from each other have the meaning of H or lower alkyl,
X	has the meaning of imino, oxa or thia;
Y	has the meaning of hydrogene, unsubstituted or substituted aryl, heteroaryl, or unsubstituted or substituted cycloalkyl; and
Z	has the meaning of amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherificated or esterificated hydroxy, nitro, cyano, carboxy, esterificated carboxy, alkanoyl, carbamoyl, N-mono- or N, N- disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower-alkyl-thio, alkyl-phenyl-thio, phenylsulfinyl, phenyl-lower-alkyl-sulfinyl, alkylphenylsulfinyl, phenylsulfonyl, phenyl-lower-alkan-sulfonyl, or alkylphenylsulfonyl,

whereas, if more than one rest Z is present ( $m \geq 2$ ), the substituents Z are equal or different from each other,

and

wherein the bonds marked with an arrow are single or double bonds; or an N-oxide of said compound, wherein one ore more N-atoms carry an oxygene atom, or a salt thereof,

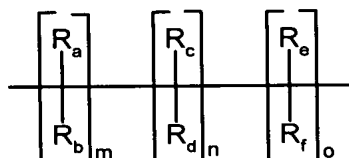
and/or a compound of general formula IV



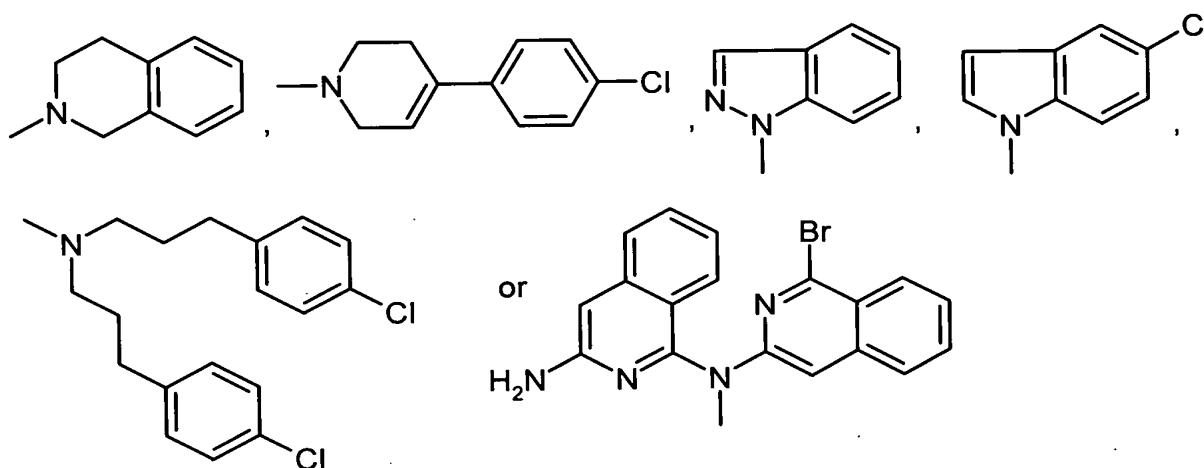
IV

in which

- A has the meaning of group  $=NR^2$ ,  
 W has the meaning of oxygen, sulfur, two hydrogen atoms or the group  $=NR^8$ ,  
 Z has the meaning of the group  $=NR^{10}$  or  $=N-$ ,  $-N(R^{10})-(CH_2)_q-$ , branched or unbranched  $C_{1-6}$ -Alkyl or is the group



or A, Z and  $R^1$  together form the group



m, n and o

q

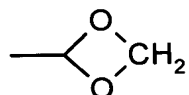
$R_a$ ,  $R_b$ ,  $R_c$ ,  $R_d$ ,  $R_e$ ,  $R_f$

has the meaning of 0 – 3,

has the meaning of 1 – 6,

independently from each other have the meaning of hydrogen,  $C_{1-4}$  alkyl or the group  $=NR^{10}$ , and/ or  $R_a$  and/ or  $R_b$  together with  $R_c$  and or  $R_d$  or  $R_c$  together with  $R_e$  and/ or  $R_f$  form a bound, or up to two of the groups  $R_a$ - $R_f$  form a bridge with each up to 3 C-atoms with  $R^1$  or  $R^2$ ,

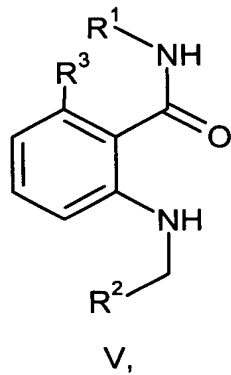
- X has the meaning of group =NR<sup>9</sup> or =N-,
- Y has the meaning of group -(CH<sub>2</sub>)<sub>p</sub>,
- p has the meaning of integer 1-4,
- R<sup>1</sup> has the meaning of unsubstituted or optionally substituted with one or more of halogene, C<sub>1-6</sub>-alkyl, or C<sub>1-6</sub>-alkyl or C<sub>1-6</sub>-alkoxy, which is optionally substituted by one or more of halogen, or is unsubstituted or substituted aryl or heteroaryl,
- R<sup>2</sup> has the meaning of hydrogen or C<sub>1-6</sub>-alkyl, or form a bridge with up to 3 ring atoms with R<sub>a</sub>-R<sub>f</sub> together with Z or R<sub>1</sub>,
- R<sup>3</sup> has the meaning of monocyclic or bicyclic aryl or heteroaryl which is unsubstituted or optionally substituted with one or more of für halogen, C<sub>1-6</sub>-alkyl, C<sub>1-6</sub>-alkoxy or hydroxy,
- R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup> and R<sup>7</sup> independently from each other have the meaning of hydrogen, halogene or C<sub>1-6</sub>-alkoxy, C<sub>1-6</sub>-alkyl or C<sub>1-6</sub>-carboxyalkyl, which are unsubstituted or optionally substituted with one or more of halogene, or R<sup>5</sup> and R<sup>6</sup> together form the group



- R<sup>8</sup>, R<sup>9</sup> and R<sup>10</sup> independently from each other have the meaning of hydrogen or C<sub>1-6</sub>-alkyl, as well as their isomers and salts,

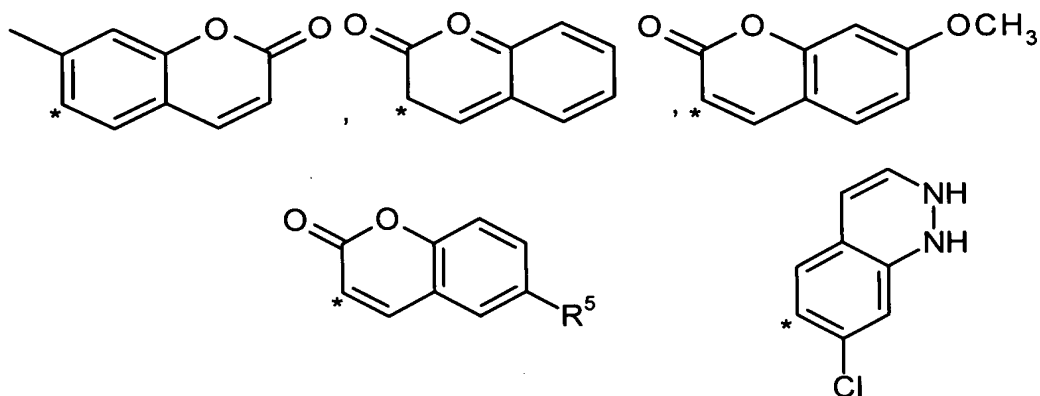
and/ or a compound of general formula V



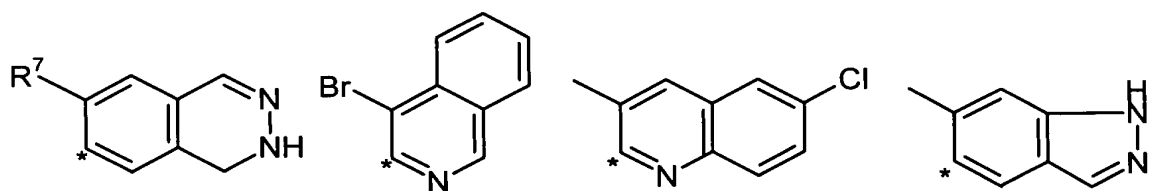


in which

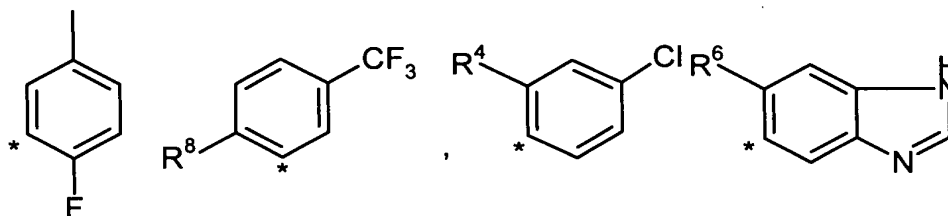
$R^1$  has the meaning of group



in which  $R^5$  is chloro, bromo or the group  $-OCH_3$ ,



in which  $R^7$  is  $-CH_3$  or chloro,

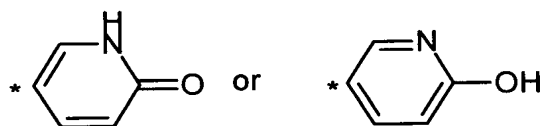


in which  $R^8$  is -CH<sub>3</sub>, fluoro, chloro, or -CF<sub>3</sub>,

in which  $R^4$  is fluoro, chloro, bromo, -CF<sub>3</sub>, -N=C, -CH<sub>3</sub>, -OCF<sub>3</sub> or -CH<sub>2</sub>OH

in which  $R^6$  is -CH<sub>3</sub> or chloro

$R^2$  has the meaning of pyridyl or the group



and

$R^3$  has the meaning of hydrogen or fluoro,

as well as their isomers and salts.

**Claim 16. (Withdrawn)** Pharmaceutical compositions according to claim 15 which comprise as compound I and/or II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate.

**Claim 17. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, and as compound II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, with the provision that compound I is not identically to compound II.

**Claim 18. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium

hydrogen succinate and as compound II sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate.

**Claim 19. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I mAB 4301-42-35 and as compound II sTie2, and/ or scFv-tTF conjugate.

**Claim 20. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I scFv-tTF conjugate and as compound II sTie2 and/ or mAB 4301-42-35.

**Claim 21. (Withdrawn)** Pharmaceutical compositions according to claim 1 which comprise as compound I L19 scFv-tTF conjugate and as compound II sTie2.

**Claim 22. (Withdrawn)** Use of pharmaceutical compositions according to claim 1, for the production of a medicament for the treatment of tumors, cancers, psoriasis, arthritis, such as rheumatoide arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, kidney diseases, such as glomerulonephritis, diabetic nephropathie, malignant nephrosclerosis, thrombotic microangiopathic syndrome, transplantation rejections and glomerulopathy, fibrotic diseases, such as cirrhotic liver, mesangial cell proliferative diseases, arteriosclerosis, damage of nerve tissues, suppression of the ascites formation in patients and suppression of VEGF oedemas.